Amendments to the Specification:

Please replace paragraph 188 at page 43 with the following amended paragraph:

[188] Microtiter plate formats using fluorescent labels and microplate fluorometers enable femtomole-attomole sensitivities. Many types of microplate fluorometers are commercially available. Molecular Device's FLIPR® microplate fluorometer or LJJ Biosystem's ~~Acquest~~ ACQUEST™ microplate fluorometer have the ability to handle 1536-well plates and have a high degree of automation. Bio-Tek Instruments' Model FL600 microplate fluorometer can detect less than 2 femtomoles of fluorescein with a read time of 28 sec. Molecular Device's ~~SPECTRAmax Gemini~~ SPECTRAMAX GEMINI® microplate fluorometer can detect 5.0 femtomoles of FITC in 96 well plates with a read time of less than 27 sec. Instruments are also available that combine time-resolved fluorescence with fluorescence resonance energy transfer pairing. This combination requires two fluorophores emitting at different wavelengths. The first emits right away, but the second is activated only when the two are in proximity, i.e., when two labeled molecules are bound. This allows simultaneous measurement of bound and unbound analytes and thus permits internal calibration. As mentioned above, it also means that the assay is homogeneous, and therefore, it is easy to automate and miniaturize.

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Please replace paragraph 189 at page 43 with the following amended paragraph:

[189] Other detectors suitable for use in the current will depend on the label employed. The labels will be quantitatively detected in a manner appropriate to their nature, for example, by counting the radioactivity of a radioactive label or scanning a fluorescent label with a light beam. Detectors include, but are not limited to, scintillation counters, e.g., a microplate scintillation counter ~~such as TopCount (Packard)~~, gamma counters, phosphorimagers, luminometers, spectrofluorometers, spectrophotometers and others.

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Please replace paragraph 210 at page 49with the following amended paragraph:

[210] Fluorescein measurements are carried out with the excitation at or around 490 nm and emission at 520 nm. Some fluorescent labels suitable for use in the subject invention include, but are not limited to, fluorescein (FITC, DTAF (fluorescein dichlorotriazine)) (excitation maxima, 492 nm/ emission maxima 516-525 nm); carboxy fluorescein (excitation maxima, 492

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nm/emission maxima, 514-518 nm; 2=- methoxy-CF (excitation maxima, 500 nm/emission maxima, 534 nm); ~~TRITC G~~ (tetramethylrhodamine isothiocyanate, isomer G (excitation maxima, 535-545/emission maxima, 570-580); ~~RBITC~~ (rhodamine-B isothiocyanate (excitation maxima, 545-560/emission maxima, 585); ~~Texas Red~~ sulforhodamine 101 sulfonyl chloride (excitation maxima, 595/emission maxima, 615-620); Cy-5™ (~~Cyanine~~ water-soluble cyanine dye) (excitation maxima, 649/emission maxima, 670); Cy-3.5™ (water-soluble cyanine dye) (excitation maxima 581nm/ emission maxima, 596 nm); ~~XRITC~~ (rhodamine X isothiocyanate (excitation maxima, 582 nm /emission maxima, 601 nm); ethidium bromide (excitation maxima, 366 nm/ emission maxima 600 nm); ~~Thiazole~~ thiazole orange ~~(To-Pro)~~ (excitation maxima, 488 nm/emission maxima 530-580 nm).

Please replace paragraph 237 at page 58 with the following amended paragraph:

[237] In another embodiment, the synthetase-elongation factor-avidin molecule can be conjugated to a different biotinylated peptide or peptide bearing a strepa-tag sequence. The ~~Strept-tag~~ strept-tag constitutes a nine amino acid-peptide that specifically binds to streptavidin occupying the same binding site where biotin normally binds. Streptavidin tag fusion proteins can be constructed and used to immobilize proteins to streptavidin. Any ~~Affinity-Tag~~ affinity tag sequences, such as hexahistidine ~~Hexa-histidine~~ for metal chelate immobilization and epitope sequence for specific binding by an immobilized antibody, can be used. In one embodiment of the subject microarray, 20 different epitope sequences and 20 different antibodies, one that specifically binds each epitope sequence is used to array the biorecognition molecules. These conjugates are thereby arrayed onto surfaces bearing 20 different antibodies, one specific for a unique epitope on each peptide on the 20 synthetase-elongation factor-avidin conjugates. The antibodies may be arrayed to the surface using any of the microarray technologies known in the art.

Please replace paragraph 245 at page 60 with the following amended paragraph:

[245] The ~~FlowMetrix~~™ FLOWMETRIX™ flow microfluorimetry system (Luminex[[,]] Corp.) performs analysis of up to 64 different assays by using a flow cytometer. The flow cytometer analyzes individual microspheres by size and fluorescence. In this system three

fluorescent colors, orange (585nm), red (>650nm) and green (530nm), are simultaneously distinguished by the flow cytometer. Microsphere classification is determined by the orange and red florescence, whereas green fluorescence is used for labeling the probes. As each microsphere is analyzed by the detector, the microsphere is classified into its distinct analyte specific set (from the orange and red fluorescence) while simultaneously the green fluorescence on each bead is recorded. From this data, the identity and quantity of the multiple analytes are automatically determined. This technology has the potential to be faster, cheaper, and more sensitive than other array formats. For example, 512 different assays can be analyzed in a single well in a few seconds (Chandler et al, 1998, Cytometry suppl 9:40).

Please delete paragraph 250 at page 62.

Please replace paragraph 359 at page 91 with the following amended paragraph:

[359] Scintillation proximity assays are envisaged for amino acid analysis. In scintillation proximity assays a radioisotope is used as an energy donor and a scintillant-coated surface (e.g., a bead) is used as an energy acceptor. Scintillation proximity assays (SPA) are described in United States Patent No. 4,568,649 which is incorporated herein by reference. These assays are reviewed in Alouani (2000) Methods Mol Biol 138: 135-41. The EF-Tu:GTP can be bound to SPA beads (commercially available from Amersham Corp., Amersham Place, Little Chalfont, England). For example, biotinylated elongation factors may be conjugated to avidin or streptavidin coated SPA beads which are commercially available. Biotin in the form of N-hydroxysuccinimide-biotin is available from Pierce Chemical Co., Rockford, IL. This embodiment comprises an acceptor SPA beads and quantitation of AA-tRNAs on a scintillation counter (for example a microplate scintillation counter). Microtiter plate assays for amino acid analysis may comprise embedded scintillant or a coating of scintillant ~~(such as FlashPlate. TP., available from Dupont NEN.RTM., and plates available from Packard, Meriden, Conn)~~.

Please replace paragraph 438 at page 112 with the following amended paragraph:

[438] A tRNA specific for each amino acid to be analyzed in the bead array is immobilized to a unique bead set. Uniquely distinguishable beads are commercially available (For example,

polystyrene microspheres with various surface chemistries suitable for protein and nucleic acid immobilization may be purchased from Luminex, Corporation, Austin, TX or from Bangs Laboratories, Inc., Carmel, IN). Numerous methods exist for coupling macromolecules to surface groups on beads as taught, for example, in Lundbald, 1991, *Chemical Reagents for Protein Modification* 2nd ed, CRC Press, Boca Raton, FL. For example, heterobifunctional crosslinking reagents may be used for covalent coupling. A water-soluble carbodiimide which reacts with a carboxylic acid group on the bead and an amine group in the protein or nucleic acid may be employed. Another method uses an NHS-maleimide which reacts with an amine on the bead surface and a free sulfhydryl group on the molecule to be attached. These covalent coupling groups can also be used to attach intermediate reagents such as avidin for the attachment of biotinylated molecules, or an antibody which captures the analyte to be measured.

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A probe that specifically binds AA-tRNAs such as EF-Tu:GTP is labeled with a fluorescent dye. For example, EF-Tu:GTP may be labeled with a green fluorescent dye ~~(such as BODIPY, Molecular Probes, or fluorescein isothiocyanate)~~ when the beads are distinguished by red and orange fluorescence~~, as is the case for the beads available from Luminex~~. By mixing the different sets of beads bearing the unique tRNAs, the assay will measure multiple amino acids in a sample in a single vessel (e.g., microwell or microchannel). The bead-tRNAs are then reacted with the aminoacyl-tRNA synthetases and amino acid sample in reaction buffer along with or followed by the fluorescent EF-Tu:GTP probe. The synthetases attach cognate amino acids in the sample to their specific tRNAs, each on a unique bead set, forming AA-tRNA-beads. The green fluorescent labeled EF-Tu:GTP binds the AA-tRNAs formed on each bead. After a short incubation period, the mixture of beads which now have various amounts of green fluorescence on their surface due to the binding of EF-Tu:GTP-green dye to the AA-tRNAs, are analyzed in a flow cytometer. Data acquisition, analysis, and reporting may be performed, for example, as described in Fulton et al, 1997 supra when using the bead sets available from Luminex. Using this approach, each bead is classified into its unique set on the basis of orange and red fluorescence and the green fluorescence value, corresponding to the amount of amino acid in the sample cognate to the tRNA on each bead type, is recorded.

Please replace paragraph 442 at page 114 with the following amended paragraph:

[442] The amino acid-AMP-synthetase complexes may be detected using a flow cytometer, as described above for tRNA bead arrays. For example, the beads may be read in a ~~FlowMetrix™~~ FLOWMETRIX™ or ~~Luminix^{100} system~~ LUMINEX® flow cytometry systems (Luminex Corporation, Austin, TX: www. Luminexcorp.com). The ~~FlowMetrix~~ FLOWMETRIX™ flow cytometry system may be configured for the Becton Dickinson (San Jose, CA) ~~FACScan^{R}~~ FACSCAN® flow cytometer based on a single 488-nm excitation laser. The flow cytometer analyzes individual microspheres by size and fluorescence, distinguishing three fluorescent colors, orange (585 nm), red (>650 nm) and green (530nm). Using the LUMINEX® ~~Luminex~~ 100 ~~analyzer~~analyzer, each bead set may be distinguished by a unique spectral address based on its 658nm/712nm emission ratio when excited by the 635nm laser in the LUMINEX® ~~Luminex~~ 100 instrument. The LUMINEX® ~~Luminex~~ software uses this spectral profile to assign beads to their classification. Thus, multiple bead classifications can be combined in one sample, and the LUMINEX® ~~Luminex~~ software processes the signals to generate an array. In the LUMINEX® ~~Luminex~~ 100 analyzer, determination of the amounts of amino acid bound to each bead classification may be accomplished by coincident excitation of the beads with the 532nm laser in the instrument. Thus, labeling bead bearing amino acid complexes with a green fluorescent reporter such as phycoerythrin (Molecular Probes, Eugene, OR) which emits at 575 nm when excited at 532 nm, produces a third fluorescent signal that allows the amount of amino acids bound to the beads to be quantitated.

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Please replace paragraph 450 at page 116 with the following amended paragraph:

[450] In a further embodiment of the method, an aminoacyl-tRNA is complexed with an elongation factor and the complex of the aminoacyl-tRNA with the elongation factor is determined. The complexing reaction buffer and conditions used to form the ternary complex will be according to the elongation factor used. Suitable reaction buffers and conditions are well known to those of skill in the art. The elongation factor preferably should be in molar excess over the aminoacyl tRNA formed. The amount therefore ~~depednds~~ depends upon the amount of amino acid in a sample. Dynamic range finding methods which are well known to one of

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A9 cont.

ordinary skill in the art can be used to empirically ascertain the optimum amounts of reactants, synthetase, and elongation factor in an assay.